UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,203	06/29/2006	Simon Michael West	22380-014US1 / FP24072	4056

26161 7590 04/11/2008
FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
MAEWALL, SNIGDHA	
ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
04/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,203	WEST ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. Receipt of Applicants Arguments/Remarks, Amended Claims and RCE, all filed on 03/07/08 is acknowledged.

Claims 16-18 have been amended. Claims 19-20 remain cancelled.

Claims 1-18 and 21-24 are pending in this application and **claims 1-18 and 21-24** will be prosecuted on the merits.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-4, 6-18 and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kirby et al. U.S.Patent No. 6,444,234 B1 (herein after '234) in view of WO 02/40033 A1 (herein after '033) and further in view of Vaghefi et al.(US PG pub 2003/0157326).

Kirby et al. discloses pharmaceutical compositions for the transdermal administration of a medicament or active agent by topical application of the composition to the skin of humans or animals (abstract).

'(234) teaches a method for formulating safe and effective compositions for topical transdermal applications of an active agent such as morphine (column 5 lines 3-5 and col. 42 example 14). The composition as set forth by ('234) comprises an active agent in a "carrier". Said "carrier" comprises solvent and modifying agents. The solvent modifiers facilitate the dissolution of the active agent and formation of the weak association which enable the complex of active agent-modifier to pass the defensive of the skin with minimal irritation without modification of the chemical structure or stereoscopic configuration of the active agent (column 11, lines 5-10). The solvent modifiers selected do not form permanent or strong covalent bonds with the medicament or active agents; instead they form complexes that facilitate the movement of the complex past the viable skin to its targeted site (column 5 lines 53-56).

Although ('234) discloses the use of solvent modifiers in formulating pharmaceutical

compositions for the transdermal administration of a medicament or active agent, ('234) does not explicitly teach using phosphate derivatives of tocopherol or other tocols as claimed in the instant application as solvent modifiers for the same purpose.

However, WO 02/40033 A1 ('033) teaches an efficacious therapeutic emulsion formulation for therapeutic administration comprising phosphate derivatives of "electron transfer agents" and an "acceptable carrier" (abstract).
According to ('033), the use of a phosphorylated electron transfer agent plays therapeutic and efficacious role in dermal penetration (page 3, lines 3-8).The "electron transfer agents" as indicated by ('033), refer to the class of chemicals, which may be phosphorylated. Examples of classes of "electron transfer agents" that may be phosphorylated include hydroxyl chromans including alpha, beta and gamma tocopherol, tocols and tocotrienols in enantiomeric and racemic forms; quinols being the reduced form of vitamin K1 and ubiquinone; hydroxyl carotenoids including retinol and ascorbic acid (page 3, lines 26-28 and page 4, lines 1-2). The phosphate derivatives may exist in the form of a free phosphate acid, a salt thereof, a di-phosphate ester thereby including two molecules of electron transfer agents, a mixed ester including two different compounds selected from electron transfer agents, or a phosphatidyl compound (page 4, lines 5-9). ('033) further teaches that the phosphate derivatives of "electron transfer agents" can be combined with 'acceptable carrier". As defined in ('033), the "acceptable carrier" could be referred to a "carrier" considered by those skilled in the drug, food or cosmetic arts to be non-toxic when used to treat humans,

animals or plants in parenteral or enteral formulations. The “carrier” will depend on the route of administration and the ingestible formulations, which include tablets, capsules, powders etc. (see page 4, lines 30-33 and page 5, lines 1-6). (‘033) further teaches that phosphate derivative may exist in the form of a phosphatidyl compound wherein the free phosphate oxygen forms a bond with an alkyl group or a complex with a complexing agent selected from amphoteric surfactant, cationic surfactant or aminoacids having nitrogen functional groups or proteins rich in these amino acids (see page 4, lines 8-11 and claim 4)._‘033teaches electron transfer agents comprising phosphate complexes of tocopherol, the usefulness of these compounds in therapeutic formulations due to their enhanced absorption properties (see full document, specifically Page 3, line 22-Page 4, line 2, Page 5, paragraph 3-Page 6, paragraph 5, Pages 7-9, Example 2, Table 1).

Vaghefi et al. while disclosing absorption enhancing pharmaceutical compositions and methods, teach tocopherol phosphate as bio enhancer (see page 5 paragraph {0045]). Vaghefi et al. further disclose that small molecule drugs that exhibit limited bioavailability in humans and that are capable of being formulated into a higher bioavailable composition and used to provide better bioavailability are administration include alkaloids such as codeine, fentanyl and quinine etc. (see page 9, paragraph [0094]).

(Instant specification teaches that most alkaloids are not water soluble. Typically alkaloids are a class of drugs that are not commonly administered transdermally because the hydrophilic nature of alakaloid salts ususally limits transdermal transport. (see page 2, lines 10-15).

Based on the foregoing, it would have been obvious to one of ordinary skilled in the art at the time of the invention to use the phosphate derivatives of tocopherol ('033) in the compositions of (‘234) comprising an alkaloid such as morphine or any other alkaloid such as codeine, fentanyl and quinine. One skilled in the art would have been motivated to utilize tocopherol phosphate with alkaloid because ‘033 teaches electron transfer agents comprising phosphate complexes of tocopherol, the usefulness of these compounds in therapeutic formulations due to their enhanced absorption properties (see full document, specifically Page 3, line 22-Page 4, line 2, Page 5, paragraph 3-Page 6, paragraph 5, Pages 7-9, Example 2, Table 1) and Vaghefi et al. teaches compositions of drugs with limited bioavailability (for instance codeine, fentanyl etc. which are known alkaloids) comprising bioenhancers such as tocopherol phosphate. Formulation of reaction product complex of morphine (or any other alkaloid) and tocopherol phosphate (electron transfer agent) would have been obvious to one of ordinary skilled in the at the time of instant invention based on the teachings of ‘033 which teaches unexpected absorption properties of the drug and Vaghefi et al. which teaches absorption enhancing composition of drugs with limited bioavailability comprising bioenhancers such as tocopherol phosphate with a reasonable expectation of success.

4. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Kirby et al. U.S.Patent No. 6,444,234 B1 (herein after ‘234) in view of WO 02/40033 A1 (“033), Vaghefi et al..(US PG pub 2003/0157326) and further in view

of Fisher et al. (US 2004/0234602 A1).

The references discussed above do not teach using enteric coatings in the oral formulations.

However, Fischer et al. in US publication (U.S. 2004/0234602 A1) discloses a composition with enteric coating and a method for controlling the release of a therapeutically active substance from a pharmaceutical composition into an aqueous medium, wherein the pharmaceutical composition is a coated matrix composition in which the matrix comprises:

Polymer or mixture of polymers,
An active substance and optionally,
One or more excipients
(Page 1, paragraph 1)
The polymers such as polyethylene oxide or eudragit L methyl ester as disclosed by Fischer et al. (on page 3, paragraph 41 and 43) are an example of enteric coatings. The active substance such as morphine, codeine and atropin can be used in the above composition (page 4, paragraph 51) in an oral formulation (page 3, paragraph 48). ('172) further teaches that in order to soften the "carrier system", a plasticizer can be selected from group of phosphate esters for e.g. a-tocopherylphosphate esters (page 8 paragraph 100).

Because Fischer et al. teaches that enteral coatings can be used to control release of drug and since it is well known in the art that enteral coatings are used to promote absorption of drugs in the intestine, it would have been obvious to one of ordinary skilled in the art at the time the invention was made to use enteric coatings as taught by Fischer et al. in the teachings advanced by Kirby et al. as modified by ('033) and

Vaghefi et al.. A skilled artisan would be motivated to prepare enteric-coated oral formulations of alkaloids such as morphine or atropine complexed with phosphate derivatives of "electron transfer agents" or in other words phosphate derivatives of tocopherol with reasonable expectations of success because enteric coatings help in the absorption of the active substance in the intestine.

Response to Arguments

5. Applicant's arguments with respect to claims 1-18 and 21-24 have been considered but are moot in view of the new ground(s) of rejection.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0580. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/

Primary Examiner, Art Unit 1612

/Snigdha Maewall/

Examiner, Art Unit 1612